REMARKS/ARGUMENTS

Claims 58-63, 69 and 70 are pending in this application.

I. Claim Rejections Under 35 U.S.C. §§101 and 112, First Paragraph (Enablement)

Claims 58-63 and 69 and 70 remain rejected under 35 U.S.C. §101 allegedly "because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility." (Page 2 of the Final Office Action mailed February 8, 2006.)

Claims 58-63 and 69 and 70 further remain rejected under 35 U.S.C. §112, first paragraph, allegedly "since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." (Page 3 of the Final Office Action mailed February 8, 2006.)

Applicants submit that, as discussed in the Responses filed on October 4, 2004, May 23, 2005, and November 18, 2005, and the Preliminary Amendment filed July 7, 2006, not only has the PTO not established a *prima facie* case for lack of utility, but the polypeptides of Claims 58-63 and 69-70 possess a specific and substantial asserted utility, and based upon this utility, one of skill in the art would know how to use the claimed polypeptides without any further experimentation.

As discussed in the Preliminary Amendment filed July 7, 2006, Applicants respectfully submit that the gene amplification data disclosed in Example 114 establishes a specific, substantial and credible utility for the PRO213-1 polypeptide. In particular, Example 114 discloses that the gene encoding the PRO213-1 polypeptide is significantly amplified in human lung and colon tumors. Table 8 explicitly states that the gene encoding the PRO213-1 polypeptide is significantly amplified, by 2.04 fold to 46.9-fold, in 35 different lung and colon primary tumors and tumor cell lines. These data demonstrate that the PRO213-1 polypeptide of the present invention is useful as a diagnostic marker for the presence of one or more cancerous tumors in which its encoding gene is amplified. Applicants respectfully submit that the above disclosure is sufficient to establish a specific, substantial and credible utility for the claimed PRO213-1 polypeptides.

One of the major issues raised by the Examiner in the Final Office Action mailed February 8, 2006, is whether in general, if a gene is overexpressed in cancer, it is more likely than not that the encoded protein will be also be expressed at an elevated level.

Applicants have previously submitted, with their Response filed October 4, 2004, a Declaration by Dr. Polakis, stating that "it remains a central dogma in molecular biology that increased mRNA levels are predictive of corresponding increased levels of the encoded protein." Applicants have also previously submitted, with their Preliminary Amendment filed July 7, 2006, a second Declaration by Dr. Polakis (Polakis II) that presents evidentiary data in Exhibit B, showing that about 90% of the genes tested according to the Polakis Declaration had a good correlation between tumor mRNA and tumor protein levels.

Applicants further enclose herewith a Declaration by Dr. Randy Scott ("the Scott Declaration"). Dr. Scott was a co-founder of Incyte Pharmaceuticals, Inc., the world's first genomic information business, and is currently the Chairman and Chief Executive Officer of Genomic Health, Inc., a life sciences company located in Redwood City, California, which provides individualized information on the likelihood of disease recurrence and response to certain types of therapy using gene expression profiling. Based on his more than 15 years of personal experience with the DNA microarray technique and its various uses in the diagnostic and therapeutic fields, and his familiarity with the relevant art, Dr. Scott unequivocally confirms that, as a general rule, there is a good correlation between mRNA and protein levels in a particular tissue.

As stated in paragraph 8 of the Scott Declaration:

> DNA microarray analysis has been extensively used in drug development and in diagnosis of various diseases. ..... Due to its importance in drug discovery and in the field of diagnostics, microarray technology has not only become a laboratory mainstay but also created a world-wide market of over $600 million in the year of 2005. A long line of companies, including Incyte, Affymetrix, Agilent, Applied Biosystems, and Amersham Biosciences, made microarray technology a core of their business.

In paragraph 10 of his Declaration, Dr. Scott explains the reasons for the wide-spread use and impressive commercial success of this technique, stating:

> One reason for the success and wide-spread use of the DNA microarray technique, which has led to the emergence of a new industry, is that generally there is a good correlation between mRNA levels determined by microarray analysis and expression levels of the translated protein. Although there are some exceptions on an individual gene basis, **it has been a consensus in the scientific community that elevated mRNA levels are good predictors of increased abundance of the corresponding translated proteins in a particular tissue.** Therefore, diagnostic markers and drug candidates can be readily and efficiently

screened and identified using this technique, without the need to directly measure individual protein expression levels.

(Emphasis added.)

The Declaration, which is based on Dr. Scott's unparalleled experience with both the microarray technique and its industrial and clinical applications, supports Applicants' position that microarray technology is not only mature, reliable and well-accepted in the art, but also has been extensively used in drug development and in diagnosis of various diseases and produced enormous commercial success. Therefore, if a gene, such as the gene encoding the PRO213-1 polypeptide, has been identified to be over-expressed in a certain disease, such as lung or colon cancer, it is more likely than not that the protein product is also overexpressed in the disease.

Based on the above arguments, Applicants have clearly demonstrated a credible, specific and substantial asserted utility for the PRO213-1 polypeptides, for example, as diagnostic markers for lung or colon tumors. Further, based on this utility and the disclosure in the specification, one skilled in the art at the time the application was filed would know how to use the claimed polypeptides.

Applicants therefore respectfully request withdrawal of the rejections of Claims 58-63, 69 and 70 under 35 U.S.C. §101 and 35 U.S.C. §112, first paragraph.

CONCLUSION

In conclusion, the present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should there be any further issues outstanding, the Examiner is invited to contact the undersigned agent at the telephone number shown below.

Although no fees are due, the Commissioner is hereby authorized to charge any fees, including any fees for extension of time, or credit overpayment to Deposit Account No. **08-1641**, referencing Attorney's Docket No. **39780-2630 P1C4**. Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: September 6, 2006

By: _____
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